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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/984,476	12/03/1997	M MICHAEL WOLFE	34477.2	2213

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/984,476	WOLFE ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *86-116* is/are pending in the application.

4a) Of the above claim(s) *93,95-98 and 105-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *86-92,94 and 99-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *86-116* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0105*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 01/26/2005 has been entered. Claims 86-116 are pending.

Election/Restrictions

Newly submitted claims 111-116 are directed to or encompass an invention that is independent or distinct from the invention originally claimed for the following reasons: Newly submitted claims 111-116 are directed to or encompass an antibody, classified in class 424, subclass 130.1. The invention originally claimed is drawn to a GIP antagonist, classified in class 530, subclass 326.

The invention originally claimed is related to the antibody of the newly submitted claims by virtue of being the cognate antigen, necessary for the production of the antibody. Although the invention originally claimed and antibody are related due to the necessary stearic complementarity of the two, they are distinct inventions because they are physically and functionally distinct chemical entities. The invention originally claimed can be used in another materially different process from the use for production of the antibody, such as in a pharmaceutical composition in its own right. The antibody can be used in another materially different process from the use for antagonism of the invention originally claimed, such as in immunoaffinity purification of the cognate antigen. Furthermore, searching both inventions together would impose a serious search burden. The inventions have a separate status in the art as shown by their different classifications. A polypeptide and an antibody which binds to the polypeptide require different searches. An amino acid sequence search of the full-length amino acid sequence is necessary for a determination of novelty and unobviousness of the protein.

However, such a search is not required to identify antibodies that bind the amino acid sequence. Furthermore, antibodies which bind to an epitope of an amino acid sequence may be known even if the amino acid sequence is novel. In addition, the technical literature search for an amino acid sequence and an antibody that binds the amino acid sequence are not coextensive, e.g., antibodies may be characterized in the technical literature prior to discovery of or sequence of their binding target.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 111-116 are withdrawn from consideration as being drawn to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Newly submitted claim 93 is directed to or encompass an invention that is independent or distinct from the invention originally claimed for the following reasons: Newly submitted claim 93 is directed to or encompasses a method of identifying an antagonist of GIP receptor, classified in class 435, subclass 7.2. The invention originally claimed is drawn to a GIP antagonist, classified in class 530, subclass 326.

The invention originally claimed and newly submitted claim 93 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case The invention originally

claimed can be used in an immunization protocol for the production of antibodies or in a method of reducing postprandial insulin levels or glucose absorption in a host.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 93 is withdrawn from consideration as being drawn to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Newly submitted claims 95-98, 105-110 are directed to or encompass an invention that is independent or distinct from the invention originally claimed for the following reasons: Newly submitted claims 95-98, 105-110 directed to or encompass a method of reducing postprandial insulin levels or glucose absorption in a host, classified in class 514, subclass 12. The invention originally claimed is drawn to a GIP antagonist, classified in class 530, subclass 326.

The invention originally claimed and newly submitted claims 95-98, 105-110 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case The invention originally claimed can be used in an immunization protocol for the production of antibodies or in a method of identifying an antagonist of GIP receptor.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

on the merits. Accordingly, claims 95-98, 105-110 are withdrawn from consideration as being drawn to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's arguments with respect to claims 1, 8-16, 18-40, 43-55, 60-78, 80-82 have been considered but are moot in view of the new ground(s) of rejection.

Maintained Formal Matters, Objections, and/or Rejections:

Double Patenting

Claims 86-92, 94, 99-104 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 36-45, 51, 53, 55, 58-67, 73, 75, 77, 83, 85 of copending Application No. 10/003,674. Applicants state that they reserve the right to respond as such time as is appropriate. It should be kept in mind that applicants cannot, as a matter of right, amend any finally rejected claims, add new claims after a final rejection (see 37 CFR 1.116) or reinstate previously canceled claims.

New Formal Matters, Objections, and/or Rejections:

Claim Objections

Claims 87-92, 100-104 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 87-92, 100-104 depend, directly or indirectly, from claim 86. Claim 86 "consists of SEQ ID NO: 5". A claim which depends from

a claim which "consists of" of a recited amino acid sequence cannot add to or change the recited amino acid sequence. Claims 87-92, 100-104 change the amino acid sequence of SEQ ID NO: 5. For the purposes of determining the patentability of these claims the examiner has interpreted the claims as consisting of the indicated sequence. This interpretation of the claims by the examiner does not relieve Applicants from responding the present objection.

Claims 90 and 91 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits. Claim 91 is a multiple dependent claim because it depends from claim 90, which is a multiple dependent claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 99 is rejected under 35 U.S.C. 102(b) as being anticipated by Moody (U).

Moody discloses the isolation of GIP (Abstract and Section 3.1, pages 144-145). GIP comprises the amino acid sequence of SEQ ID NO: 5, as indicated below (Qy = SEQ ID NO: 5) (Db = GIP):

```
Qy       1 YSIAMDKIHQQDFVNWLLAQK 21
           |||||||||||||||||||||
Db      10 YSIAMDKIHQQDFVNWLLAQK 30.
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Accordingly, Moody discloses an isolated polypeptide comprising a 21-residue sequence at least 95% identical to SEQ ID NO: 5.

Claim 94 is rejected under 35 U.S.C. 102(b) as being anticipated by Ebert (Endocrinology. 1982 Nov;111(5):1601-6).

Ebert discloses a GIP antiserum or antibody that completely blocked the insulinotropic effect of exogenous porcine GIP (page 1601, Abstract). Accordingly, Ebert's GIP antiserum or antibody is a GIP antagonists. According to the present specification, a GIP antagonist is any composition which interferes with biological action of GIP. Such compositions include antibodies specific for either GIP or GIP receptors. Page 7, last full paragraph. Therefore, it is reasonable to construe a "GIP receptor antagonist" as a GIP antagonist. Also, claim 94 directed to a product produced by the process of claim 93. Ebert does not describe production of the GIP antiserum or antibody using methods identical to that recited in claim 93. However, the process limitation in claim 93 is not viewed as positively limiting the product of claim 94 since it is assumed that equivalent products are obtainable by multiple routes. The burden is upon the applicants to establish a patentable distinction between the claimed GIP receptor antagonist and Ebert's GIP antiserum or antibody.

Claim Rejections - 35 USC § 112

Claim 94 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is directed to or encompasses a GIP receptor antagonist that is produced by the process of claim 93. The process of claim 93 is not viewed as positively limiting the antagonist of claim 94 absent a showing that the process imparts a novel or unexpected property to the antagonist, as it is assumed that equivalent products are obtainable by multiple routes.

The present specification defines a GIP antagonist as "any composition which interferes with biological action of GIP. Such compositions include antibodies specific for either GIP or GIP receptors, antisense RNA which hybridizes with mRNA encoding GIP or GIP receptor, or other genetic controls which knock out expression of GIP or GIP receptor. GIP antagonists also include peptides or other small molecules which bind to the GIP receptor and block the cAMP response to GIP." Page 7, paragraph 32.

There are no structural limitations to the antagonist claimed in claim 94. Accordingly, claim 94 is directed to a genus encompassing products defined only by what they do rather than by what they are. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The specification and claim do not place any limit on the structure of the claimed product. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Structural features that could distinguish compounds in the genus are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the

disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claims 87, 90, 94, 99-104 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following limitations are not supported by the original disclosure and they introduce new concepts, thereby violating the written description requirement of 35 U.S.C. § 112, first paragraph:

Lys at position 9 (claims 87, 104);

the method of claim 93, hence the product produced by the method of claim 93 (claim 94);

neutral amino acid or different neutral amino acid (claims 100, 101);

the indicated substitutions of a neutral amino acid at the indicated positions (claims 100, 101);

the indicated substitutions of Asp at the indicated positions (claims 102, 103);

a composition comprising both the polypeptide of claim 86 and the polypeptide of claim 88 (claim 90);

at least 95% identical to the corresponding amino acids of SEQ ID NO: 5 (claim 99).

Claim 99 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to or encompass a polypeptide at least 95% identical to the corresponding amino acids of SEQ ID NO: 5. The claims do not require that the polypeptide possess any particular biological activity, nor any particular conserved structure, or other disclosed distinguishing feature. Thus, the claims are drawn to a genus of polypeptides that is defined only by sequence identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of a recitation of percent identity. There is not even identification of any particular portion of the structure that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in

possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 5, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 87, 99-104 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polypeptide consisting of the amino acid sequence of

SEQ ID NO: 5, does not reasonably provide enablement for the indicated polypeptides without regard to their functional activity. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to a polypeptide at least 95% identical to SEQ ID NO: 5 (claim 99) or having specified amino acid substitutions with respect to SEQ ID NO: 5 (claims 100, 101). The present specification exemplifies the following four GIP antagonists:

```
SEQ ID NO: 2        1 ISDYSIAMDKIHQQDFVNWLLAQK 24
SEQ ID NO: 5          1 YSIAMDKIHQQDFVNWLLAQK 21
SEQ ID NO: 8        1 ISDYSIAMDKIRQQDFVNWLLAQK 24
SEQ ID NO: 10         1 YSIAMDKIRQQDFVNWLLAQK 21.
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As can be seen, these four antagonist differ by a single amino acid residue. Yet the claims are directed to or encompass polypeptides that differ at any amino acid from these four highly similar antagonists (claim 99) or have other selected amino acid substitutions (claims 100-104) or have a Lys residue instead of His or Arg residue at position 9 (claim 87). There is no functional limitation in the claims.

The skilled artisan would not know how to use polypeptides not identical to SEQ ID NO: 5 unless they possessed the disclosed antagonistic function. The specification does not provide guidance for using polypeptides related to (e.g., 95% identity) but not identical to SEQ ID NO: 5. The claims are broad because they do not require the claimed polypeptide to be identical to the disclosed sequence and because the claims have no functional limitation. The skilled artisan is left to an extensive amount of undue experimentation wherein polypeptides at least 95% identical to SEQ ID NO: 5 or polypeptides having the indicated substitutions are randomly made and/or randomly tested for a useful function. Moreover, there is a lack of predictability in the

art. Predicting structure, hence function, from primary amino acid sequence data is extremely complex and there doesn't exist an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. See Ngo (U, Paper No. 6) page 433, full paragraph 1, and page 492, full paragraph 2.

Because of the lack of direction or guidance for using polypeptides that are not identical to SEQ ID NO: 5 and the breadth of the claims for structure without function, it would require undue experimentation to use the invention commensurate in scope with the claims.

Claim 94 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling a polypeptide consisting of the amino acid sequence of SEQ ID NO: 5, does not reasonably provide enablement for an antagonist of GIP receptor identified by contacting a cell that expresses a GIP receptor with a candidate compound and the polypeptide of claim 86 or claim 88 and determining whether the candidate compound competitively inhibits the binding of the polypeptide of claim 86 or claim 88 to the GIP receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claim is directed to or encompasses an antagonist of GIP receptor produced by contacting a cell that expresses a GIP receptor with a candidate compound and the polypeptide of claim 86 or claim 88 and determining whether the candidate compound competitively inhibits the binding of the polypeptide of claim 86 or claim 88 to the GIP receptor. The polypeptide of claim 86 or claim 88 is GIP receptor antagonist. Accordingly, the claims are directed to or encompass a method of identifying an antagonist of GIP receptor, by determining whether a

candidate compound competitively inhibits the binding of a GIP receptor antagonist to the GIP receptor. However, it is not predictable that a compound that competitively inhibits the binding of a GIP receptor antagonist to the GIP receptor is an antagonist of the GIP receptor because an agonist of a GIP receptor could also competitively inhibit the binding of a GIP receptor antagonist to the GIP receptor. Neither the claim nor the specification set forth the method steps required to determine whether the compound is an agonist or an antagonist. Accordingly, the claim is not enabled for the full scope of the claimed invention.

Claim 99 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear if the phrase "corresponding to" should be interpreted narrowly to encompass only materials that have a structure at least 95% identical to SEQ ID NO: 5 or if the phrase should be interpreted broadly to encompass materials which have a structure at least 95% identical to a structure similar to SEQ ID NO: 5. The metes and bounds are not clearly set forth.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

DSR
APRIL 20, 2005